REMARKS

Claims 10-13, 17, 21-25, and 27 stand rejected under 35 U.S.C. 102(b) as being anticipated by T.G. Ewart and T. Bogle, U.S. Patent 5,922,537 ("Ewart").

Claims 1-5 and 9 stand rejected under 35 U.S.C. 103(a) as being unpatentable Ewart in view of S-J. Park et al., Science, 295: 1503-1506, 2002 ("Park"). For the following reasons, these rejections should be withdrawn.

Claims 1 and 10 have been amended. Support for these amendments is found throughout the application; see, for example, paragraphs 0050, 0064, and 0089 of the published patent application. Claim 5 has been cancelled. No new matter has been added by the present amendments.

As an initial matter, Applicants thank Examiner Kingan for the productive telephonic interview conducted on March 17, 2010 with Applicants' representatives, James DeCamp and Maarten Nollen, a European patent attorney. Applicants have amended the claims as discussed during the interview and, as requested, review below several matters discussed in the interview. Applicants believe that no new search is required in view of the present amendments.

Ewart, at best, proposes a method of detection of target samples that includes reporter particles. The reporter particles may have magnetic, capacitive or fluorescent properties. The reporter particles are submicron particles of uniform dimension. The target samples are then bound on a substrate surface. Detection of the target sample is

carried out by capacitive, inductive or optical detection, as part of a competition assay method.

In connection with capacitive detection, Ewart senses a difference $\Delta C = C_1 - C_2$ (see column 13, eq. 12A and 12B). Ewart states that the change is determined exclusively by the change in dielectric constant K_d (from the particles) to K_w (from water) (column 13, line 62). Ewart concludes that the maximum ΔC is achieved with the thinnest possible passivation layer having the highest possible dielectric constant, and with dielectric nanoparticles having a dielectric constant as close as possible to 1 (column 14, lines 16-20).

As known to the skilled person, a vacuum has a dielectric permittivity (relative dielectric constant) of 1. Air has a dielectric permittivity of close to 1. Thus, Ewart effectively teaches to use 'porous' particles.

The operation of Ewart may become clearer upon reading of column 9, line 13 and beyond: "The materials useful as capacitance particle reporters ... are those which will alter the electrical resistance of the test surface. That is, these materials, if distributed as a finely divided powder on the test surface, alter the dielectric, conductive or magnetic properties of the surface." As acknowledged in column 14, Ewart preferably uses a passivation layer on the surface with a very high dielectric constant, such as bariumtitanate ($BaTiO_3$).

In other words, the particles having a low dielectric constant (and a relatively high

resistivity), will alter the electric resistance of the surface, if sufficiently many of them are bound to the surface.

In short, Ewart proposes a change in electrical properties through binding of a plurality of particles with a low dielectric constant. This would provide the largest difference with the dielectric constant of water.

Moreover, Ewart is particularly aimed at determination of a concentration in a fluid (see column 2, line 45-50 of Ewart). It does not appear appropriate for measurement of small amounts of either a low number or a large number of different molecules or molecular fragments. Such detection of a biomolecule, particularly DNA or a DNA fragment, even when present in small amounts is the object of the invention (see paragraph 0010 and the preceding discussion of the present specification).

Park et al. discloses an alternative method of detection that is more suitable for detection DNA, when present in low amounts. However, Park's method has the disadvantages that the method may not be robust (as discussed in paragraph 0007 of the present specification) and processing for manufacturing the sensor appears incompatible with conventional integrated circuit fabrication.

Applicants solve this issue by performing capacitive measurements between a pair of electrodes provided with non-conducting surfaces. To obtain a suitable result, the target samples are provided with a conductive label. This is done in such a manner that the one (or more) conductive label effectively contacts said non-conducting surface of

said electrode. The capacitive measurement then measures the capacitance of the non-conductive surface only, instead of measurement of the capacitance of a fluid including some particles with certain properties.

So, where Ewart teaches to use a plurality of particles with a low dielectric constant to reduce capacitance of a fluid-based complexing layer (i.e., formed by the fluid and the particles attached to the passivation layer, see Ewart column 13, line 34), Applicants employ a conductive label. The measured capacitance is based on the capacitance of the non-conductive surface in the area covered by the label. The claimed invention is therewith suitable for a low amount of particles, or even one of a kind, whereas Ewart focusses on a concentration measurement based on a high number of particles.

Accordingly, Ewart fails to anticipate claims 10-13, 17, 21-25, and 27.

Furthermore, even in combination, the teachings of Ewart and Park do not teach or suggest all the elements of claims 1-5 and 9.

Indeed, applicants submit that there is compelling secondary evidence of non-obviousness. Rather than rendering the claimed invention obvious, Ewart clearly teaches away from the claimed invention. Evidence rebutting a *prima face* case of obviousness can include: evidence "that the prior art teaches away from the claimed invention in any material respect," *In re Peterson*, 315 F.3d 1325, 1331 (Fed. Cir. 2003). When a patent applicant puts forth rebuttal evidence, the Office must consider that evidence. *See In re*

Soni, 54 F.3d 746, 750 (Fed. Cir. 1995) (stating that "all evidence of nonobviousness must be considered when assessing patentability"). For all of the aforementioned reasons, the Office has failed to make a *prima facie* case of obviousness. This is because a person having ordinary skill in the art would not have been motivated to combine Ewart and Park to achieve the claimed invention. In addition, even if the Office had made a *prima facie* showing, the *prima facie* case is rebutted by Ewart's teaching to use a plurality of particles with a low dielectric constant to reduce capacitance of a fluid-based complexing layer which teaches away from Applicants' use of a conductive label.

For completeness, Applicants note that claims 6, 7, 8, 14, 15, 16, 18, 19-20, and 26 stand rejected in view of Ewart in combination with one or more secondary references including Park. Applicants above remarks concerning Ewart and Park are applicable to these claims as well, and thus are patentable over these references. The rejections of these claims should, therefore, be withdrawn.

Finally, during the interview the Examiner made an inquiry into a measurement issue referring to the phrase "average to air" as found in Figure 15. To address this inquiry, Applicants note that Figures 15A, 15B, and 15C show measurements with three different sensors (Fig. 15A 2 micron distance between electrodes, Fig. 15B 6 microns, Fig. 15C 4 microns). Each figure shows capacitance as a function of frequency for three samples, after a specified period (a "relevation time" of 2 minutes 30 seconds) in which metal (silver) was bound by precipitation on the deposition initiator: - sample 1: no DNA

(= witness); sample 2: DNA concentration of 0.2 nMol (= nmol per liter); and sample 3: DNA concentration of 20 nMol (= nmol per liter).

The "average to air" is the result of the measurement of the sensor in air, instead of in medium with or without DNA. Each "average to air" line is based on measurements of three sensors (each having the same electrode distance). It is thus a reference. Applicants also point out that an explanation of "average to air" measurement is found in paragraph 0129 of the patent application publication.

Applicants moreover emphasize that the Figures 15A-C also demonstrate the functional results obtained according to the claimed invention. Sample 1 in each figure (no DNA) is a measurement without bound conductive label (no DNA). Samples 2 and 3 are measurements of the sensor having bound conductive labels. The difference in capacitance is excellent. Indeed, the difference in capacitance is higher for sample 3, but this also has a 100 fold higher concentration of DNA. In other words, the excellent results for sample 2 evidences that the invention allows for the measurement of DNA also when present in low concentrations.

CONCLUSION

Applicants submit that the present claims are in condition for allowance, and such action is respectfully requested.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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